SCIENTIFIC APPARATUS AND LABORATORY METHODS

PENICILLIN IN IODIZED OIL FOR INSTILLATION INTO THE LUNGS[1]

THE instillation of iodized oil as an aid in roentgen diagnosis of bronchiectasis, sinus tracts and other conditions is an established procedure. The addition of a potent anti-bacterial agent to the iodized oil might produce a valuable therapeutic aid in the above conditions.

The successful preparation and utilization of calcium penicillin in beeswax peanut oil[2, 3, 4] suggested the possibility of suspending penicillin in an iodized oil. It was necessary to establish the following facts: (1) that penicillin could be suspended in an iodized oil; (2) that iodized oil would have no adverse effect on the penicillin; (3) that the suspension would be stable, and (4) that the penicillin iodized oil would cause no damage to the tissues.

The penicillin iodized oil is prepared in the same manner as previously reported[2, 3, 4] for calcium penicillin beeswax peanut oil. Calcium penicillin is placed in a sterile mechanical blendor and a sufficient quantity of sterile 40 per cent. iodized oil is added. The mixture is blended for approximately 10 to 15 minutes. Each cc of the final suspension contains 1,500 Oxford units of penicillin per cc. The penicillin remains suspended in the mixture and does not settle.

Stability tests on the penicillin iodized oil indicate no adverse effect on the penicillin and show no deterioration when the mixture was kept at refrigerator, room and 37° C. temperatures for 60 days.

As initial experiments 8 rabbits were anesthetized and 1 to 3 cc of the penicillin iodized oil were injected through the trachea into the bronchi. Roentgen rays of the rabbits showed the penicillin iodized oil in the tracheobronchial tree. Depending on the amount of penicillin iodized oil instilled in the lungs, blood levels[5] of .039 to 1.25 Oxford units per cc were found at 15, 30 minutes, 1 and 2 hours. The rabbits were observed for a period of 2 months, at which time they were sacrificed. Gross and microscopic studies[6] of the lungs and other organs showed no abnormalities as a result of the instillation of the penicillin iodized oil into the lungs.

The practicability of treatment of pulmonary suppurative processes by the local application of penicillin iodized oil was suggested by the rabbit experiments. Ten patients with severe saccular bronchiectasis and two with pulmonary abscess were selected. The lesions in all 12 cases were confined to one lobe of the lung.

After preliminary cocainization of the posterior pharynx the supra-glottic inhalation method was employed to introduce 7 to 10 cc of the penicillin iodized oil into the diseased pulmonary lobe. Positioning of the patient with fluoroscopic visualization of the iodized oil furnished an accurate check concerning the location of the material.

No immediate or subsequent discomfort due to the mixture was observed. Although only occasional assayable levels of penicillin were found in the bloods which were taken at 15, 30 minutes and 1, 2 and 3 hours after the single instillation of the penicillin iodized oil, penicillin continued to be excreted in the urine for at least 24 hours in all patients.

Of the 12 patients who had a single bronchial instillation of the penicillin iodized oil, 2 of the cases, one bronchiectasis and the other lung abscess, had a gradual reduction in sputum by the seventh day to approximately 50 per cent. of the original amount. By the end of a two-week period, the sputum output in both cases had returned to the amount prior to treatment. In the remaining ten cases, no significant changes were noted.

It is apparent that no definite conclusions can be drawn from the clinical studies which have been discussed. The chances of curing far advanced bronchiectasis, lung abscesses or any type of chronic pulmonary suppuration by this method seem unlikely. There is, however, a distinct possibility that the bacterial flora in the diseased lungs may be altered and make subsequent surgical intervention safer. Penicillin iodized oil may also be of value as a palliative treatment in subjects who are unsuitable risks for radical treatment.

COMMENT

Others[7, 8] have previously shown that Penicillin Aerosol penetrates the lung and may be recovered from the urine. However, by this method it is neces-

[1] From the Penicillin Section, Laboratory Service and the Thoracic Surgery Section, Walter Reed General Hospital. The technical assistance of Miss Dorothy Talbot and Technician (4th Grade) Minna Levy is gratefully acknowledged.

[2] M. J. Romansky and G. E. Rittman, SCIENCE, 199: 196, September 1, 1944.

[3] M. J. Romansky and G. E. Rittman, *Bull. U. S. Army Med. Dept.*, October, 1944, p. 43.

[4] M. J. Romansky, R. J. Murphy and G. E. Rittman, *Jour. Am. Med. Asn.*, June 9, 1945, pp. 404–407.

[5] Assays of penicillin in the blood, urine and for stability were done by the methods of Rammelkamp, *Proc. Soc. Exp. Biol. and Med.*, 51: 95–97, October, 1942; G. Rake and H. Jones, *Proc. Soc. Exp. Biol. and Med.*, 54: 189, November, 1943; and W. M. M. Kirby and L. A. Rantz, *Jour. Bact.*, 48: 603, 1944.

[6] 1st Lt. Ellery M. James, pathologist at Walter Reed General Hospital, examined the sections.

[7] V. Bryson, E. Sansome and S. Laskin, SCIENCE, 100: 33–35, 1944.

[8] A. L. Barach, F. H. Silberstein, E. T. Oppenheimer, T. Hunter and M. Soroka, *Annals of Int. Med.*, 22: 485, 1945.

sary to give inhalations, as many as four to five times daily, to maintain satisfactory quantities of penicillin in the lungs. Moreover, when Penicillin Aerosol is employed radiographic control of the location of the agent is not possible.

The primary purpose of this study has been to illustrate that after a single instillation of penicillin iodized oil, penicillin is present locally in the lungs for a minimum of 24 hours, as indicated by its excretion in the urine for that period of time. Further study is necessary relative to the frequency and interval of instillation of penicillin iodized oil as well as the therapeutic possibilities.

SUMMARY

(1) A suspension of calcium penicillin in 40 per cent. iodized oil produces a stable mixture which has been instilled in the lungs of 12 patients without adverse effect and has maintained penicillin in the lung for a minimum of 24 hours, after a single instillation.

(2) The penicillin iodized oil has maintained its potency for 60 days at ice box, room and 37° C. temperatures.

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CHROMOSOME MOUNTS FOR TEMPORARY STUDY

ZIRKLE'S[1] solution, or a modification of this, as a sealing agent for the temporary preservation of chromosome mounts has been found to be more effective and more convenient than any of the various paraffin or wax and gum mastic mixtures. With a pipette a small amount of Zirkle's solution—80 cc aceto-carmine, 10 cc Karo corn syrup (Dextrose), and 10 cc Certo (Pectin)—is placed around the edges of the cover slip and allowed to dry. By this method smears of leaves,[2] root tips and anthers have been preserved in good condition for periods varying from several weeks to several months. The procedure is equally effective with propio-carmine, Feulgen, and aceto-carmine smears.

The solution has been modified by substituting 45 per cent. acetic acid for the aceto-carmine and the resulting solution used as a sealing agent. While slides so sealed do not seem to remain in good condition as long as those prepared by the first method, excellent results have been obtained with slides kept for periods up to a week or ten days. Since the possibility of over-staining which might result from the presence of Zirkle's solution around the edges of the cover slip is thereby avoided, this modified solution is suggested for slides which are to be kept for short periods.

In addition to the effectiveness of these solutions as sealing agents and the ease with which they are applied, they are also recommended, for slides sealed by them can be made into permanent mounts by removing the solution from the edges of the cover slip with a moistened cloth, by inverting the slide in acetic alcohol (1:1) until the cover slip floats off, and by following from here Meyer's[3] procedure for making smears permanent, or by using any desirable modification of McClintock's[4] permanent aceto-carmine method.

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DISCUSSION

THE LAPLACE EQUATION

THE most important partial differential equation is

$$\frac{\partial^2\phi}{\partial x^2}+\frac{\partial^2\phi}{\partial y^2}=0, \tag{1}$$

known as the Laplace equation. The applications embrace gravitation, electricity, magnetism, hydrodynamics, conduction of heat, stream lines, isothermal families, conformal mapping.

In three dimensions, the corresponding equation is

$$\frac{\partial^2\phi}{\partial x^2}+\frac{\partial^2\phi}{\partial y^2}+\frac{\partial^2\phi}{\partial z^2}=0. \tag{2}$$

This equation is much more complicated analytically; in particular the powerful method of functions of a complex variable successful for (1) is no longer available for (2).

Although the analytic difficulties are well known, we shall point out new geometric aspects. Sophus Lie found the first geometric property of isothermal families of curves in the plane. We prove that this result is no longer valid in three dimensions. From Lie's work, Kasner and De Cicco found purely intrinsic geometric properties of isothermal families and isothermal networks. These have applications to stream lines in two dimensions.

Our object is to find analogues in three dimensions.

[1] C. Zirkle, SCIENCE, 85: 528, 1937.

[2] J. T. Baldwin, Jr., SCIENCE, 90: 240, 1939.

[3] James R. Meyer, *Stain Tech.*, 18: 53–56, 1943.

[4] B. McClintock, *Stain Tech.*, 4: 53–56, 1929.